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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,484	10/21/2005	Henry Nicolas Jabbour	20747/200	4407

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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1654	

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10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,484	JABBOUR ET AL.	
	Examiner	Art Unit	
	DAVID LUKTON	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,14-17,20,21 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *7-9,14-17,20,21 and 24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Pursuant to the response filed 6/19/08, claims 10-13, 18, 19, 22, 23 have been cancelled, claim 30 added, and several claims amended. Claims 1-9, 14-17, 20, 21, 24-30 are now pending. Claims 7-29 remain withdrawn from consideration; claims 1-6 and 30 are examined in this Office action.

Applicants' arguments filed 6/19/08 have been considered and found persuasive in part.

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 30 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of treating menorrhagia. However, there is no evidence that this can be achieved by administering a $PGF_{2\alpha}$ receptor antagonist.

Applicants have shown (fig. 5) that $PGF_{2\alpha}$ can promote proliferation of endometrial adenocarcinoma cells (Ishikawa). Applicants have also shown that stained endometrial tissue obtained from women with normal blood loss looks a little different from stained endometrial tissue obtained from women with abnormally high blood loss. Perhaps

there is an argument to be made that some success could be achieved in those cases where heavy menstrual bleeding has occurred as a consequence of endometrial adenocarcinoma. However, heavy menstrual bleeding can occur for a variety of reasons, such as insufficient endothelin production or excessive PGE2 production or abnormal levels of vascular endothelial growth factor. There is also the matter of endometrial polyps and uterine fibroids to consider. Thus, in general, one can expect failure in any attempt to reduce menstrual bleeding merely by administering a $PGF_{2\alpha}$ receptor antagonist in a randomly selected case.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

There is nothing in the prior art of record to suggest that $PGF_{2\alpha}$ receptor antagonists will reduce menstrual bleeding. As for the "working examples", there is some indication that $PGF_{2\alpha}$ is somehow involved in certain types of bleeding; but there is no reason to believe that an excessive level of $PGF_{2\alpha}$ is the primary reason for the bleeding. Nor is there any reason to believe that one can select a receptor at random, and then "predict" amelioration of a given disorder. In view of the foregoing, it is

evident that "undue experimentation" would be required to practice the claimed invention.

✦

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.
>
> Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 2, 3 and 6 are rejected under 35 U.S.C. §103 as being unpatentable over Brown (USP 4,254,122) in view of any of the following: Farida (*Bangladesh Medical Research Council Bulletin* 7(2), 69-76, 1981) or Peplow P. V. (*Prostaglandins, Leukotrienes, and Essential Fatty Acids* 33(3), 239-252, 1988) or Robinson D. R. (*The Journal of Rheumatology. Supplement* 47, 32-39, 1997).

As indicated previously, Brown discloses (col 7, line 19) that inhibitors of prostaglandin synthetase such as indomethacin are effective to treat menorrhagia. Each of the

secondary references discloses that indomethacin is effective to inhibit the production of, or the activity of $PGF_{2\alpha}$. Thus, indomethacin is effective to mitigate the effect of $PGF_{2\alpha}$ on the FP receptor relative to the effect that would exist were the indomethacin absent. As for claim 3, the "interaction" is affected, because when indomethacin is administered, there is simply less $PGF_{2\alpha}$ available to "interact" with the FP receptor.

In response, applicants have acknowledged that the references would lead one to believe that prostaglandin synthetase inhibitors will be effective, not only to treat menorrhagia, but also to inhibit production of $PGF_{2\alpha}$. Applicants have then gone on to argue that the references do not disclose which of the prostaglandins are involved in menorrhagia. However, the claims do not require that one make this determination. All that is required is that one recognize that the agent he (or she) is administering will be effective to treat menorrhagia, and at the same time, to inhibit one or more pharmacological effects of $PGF_{2\alpha}$. Applicants have then gone on to state that the pharmacologist of ordinary skill would somehow come to the belief that if a given agent is effective to reduce the amount of $PGF_{2\alpha}$ that is able to make contact with the $PGF_{2\alpha}$ receptor, that agent will not be effective to mitigate the pharmacological response of the receptor to the (now) reduced level of $PGF_{2\alpha}$. However, applicants' logic is not easy to follow. Is it applicants' position that the lower the amount of agonist compound "X" that makes contact with its cognate receptor, the more the receptor will be activated? Such a notion is entirely at odds with conventional wisdom. Perhaps if claim 4 were at issue, the rejection would prove to be inadequate. But claim 4 has not been rejected.

Applicants have also begun with the premise that the rejection is not justified, and have then proceeded to argue that the invention has remained undiscovered for 20 years since the publication of Brown and Farida. However, applicants' premise is invalid; Brown in combination with Farida renders the claimed invention obvious.

Claims 1, 2, 3 and 6 are rejected under 35 U.S.C. §103 as being unpatentable over Tsang (*Can J Physiol Pharmacol* 65 2081-84 1987).

As indicated previously, Tsang discloses that mefanamic acid is effective to treat menorrhagia, and at the same time, is effective to reduce $PGF_{2\alpha}$ levels.

In response, applicants have argued that Tsang does not identify whether it is PGE or PGF that is responsible for menorrhagia. However, the claims do not require that one make this determination. If a person administers a compound that has the effect of **simultaneously** mitigating the pharmacological effects of PGE and $PGF_{2\alpha}$, and that compound is indeed effective to treat menorrhagia, the requirements of the claims are met. And if that compound has 100 other pharmacological effects in unrelated systems, the requirements of the claims are still met. What the pharmacologist (of ordinary skill) would take from the reference is that there is indeed an agent which is effective to treat menorrhagia, and at the same time, to reduce $PGF_{2\alpha}$ levels. As with the §103 above, the pharmacologist (of ordinary skill) would expect that if the amount of an agonist is reduced, the activation of its cognate receptor will also be reduced. Applicants may

believe that higher concentrations of agonists are effective to deactivate receptors, and that lower concentrations of agonists activate receptors, but this is not consistent with the perceptions of the ordinarily skilled pharmacologist.

The rejection is maintained.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

/David Lukton/

Primary Examiner, Art Unit 1654